

10/608845

We claim:

1. A method of assessing the efficacy of an obesity treatment in a subject, the method comprising:
- a) providing from the subject a test cell population comprising cells capable of expressing one or more nucleic acid sequences selected from the group consisting of OB1-6;
  - b) detecting expression of one or more of the nucleic acid sequences in said test cell population;
  - c) comparing the expression of the nucleic acid sequences in the test cell population to the expression of the nucleic acid sequences in a reference cell population comprising at least one cell whose obesity stage is known; and
  - d) identifying a difference in expression levels of the OB1-6 sequences, if present, in the test cell population and the reference cell population,
- thereby assessing the efficacy of an obesity treatment in the subject.
2. The method of claim 1, wherein the subject is a mammal.
3. The method of claim 2, wherein the subject is human.
4. The method of claim 1, wherein the method comprises comparing the expression of two or more of the nucleic acid sequences.
5. The method of claim 1, wherein the method comprises comparing the expression of four or more of the nucleic acid sequences.
6. The method of claim 1, wherein the method comprises comparing the expression of six or more of the nucleic acid sequences.
7. The method of claim 1, wherein the expression of the nucleic acid sequences in the test cell population is increased as compared to the reference cell population.
8. The method of claim 1, wherein the test cell population is provided *in vitro*.
- 9-8. The method of claim 1, wherein the test cell population is provided *ex vivo* from a mammalian subject.
- 10-9. The method of claim 1, wherein the test cell is provided *in vivo* in a mammalian subject.
- 11-10. A method of identifying a test therapeutic agent for treating obesity in a subject, the method comprising:

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- a) providing from the subject a test cell population comprising cells capable of expressing one or more nucleic acid sequences selected from the group consisting of OB1-6;
  - b) contacting said test cell population with the test therapeutic agent;
  - c) detecting the expression of one or more of the nucleic acid sequences in said test cell population;
  - d) comparing the expression of the nucleic acid sequences in the test cell population to the expression of the nucleic acid sequences in a reference cell population comprising at least one cell whose obesity stage is known; and
  - e) identifying a difference in expression levels of the OB1-6 sequences, if present, in the test cell population and the reference cell population,

thereby identifying a test therapeutic agent for treating obesity in a subject.

- 12 11. The method of claim 11 wherein the subject is a mammal.
- 13 12. The method of claim 12 wherein the subject is human.
- 14 13. The method of claim 13 wherein the test therapeutic agent is a known anti-obesity agent.
- 15 14. The method of claim 14 wherein the test therapeutic agent is selected from the group consisting of: dexfenfluramine, sibutramine, beta3-adrenergic agonists, and olistat.
- 16 15. The method of claim 15 wherein the test therapeutic agent is an unknown anti-obesity agent.
- 17 16. A method of identifying leptin-induced nucleic acid sequences, the method comprising:

- a) providing a test cell population from a subject whose obesity stage is known;
- b) measuring the expression of one or more nucleic acid sequences expressed by the test cell population;
- c) comparing the expression of the nucleic acid sequences in the test cell population to the expression of the nucleic acid sequences in a reference cell population comprising at least one cell from a subject with the opposite obesity stage;
- d) determining which nucleic acid sequences, if any, are differentially expressed in the test cell population and the reference cell population;
- e) adding leptin to the test cell population and the reference cell population;

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- f) comparing the expression of the nucleic acid sequences in the test cell population after leptin treatment with the expression of the nucleic acid sequences in the reference cell population after leptin treatment; and
  - g) identifying a difference in expression levels, if present, in the test cell population and the reference cell population,

thereby identifying leptin-induced nucleic acid sequences.

18. A method of diagnosing or determining the susceptibility to obesity in a subject, the method comprising:

- a) providing from the subject a test cell population comprising cells capable of expressing one or more nucleic acid sequences selected from the group consisting of OBs:1-6;
- b) measuring expression of one or more of the nucleic acid sequences in the test cell population;
- c) comparing the expression of the nucleic acid sequences in the test cell population to the expression of the nucleic acid sequences in a reference cell population comprising at least one cell from a subject not suffering from obesity; and
- d) identifying a difference in expression levels of the nucleic acid sequences, if present, in the test cell population and reference cell population,

thereby diagnosing or determining the susceptibility to obesity in the subject.

19. The method of claim 18 wherein the subject is a mammal.

20. The method of claim 18 wherein the subject is a human.

21. A method of treating obesity, the method comprising administering to a patient suffering from or at risk for developing obesity, an agent that modulates the expression or activity of one or more nucleic acid sequences selected from the group consisting of OBs:1-6.

22. The method of claim 21, the method comprising administering to a patient suffering from or at risk for developing obesity, an agent that decreases the expression or activity of one or more nucleic acid sequences selected from the group consisting of OBs:1, 2, 4, 5, and 6.

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22. The method of claim <sup>21</sup>20, the method comprising administering to a patient suffering from or at risk for developing obesity, an agent that increases the expression or activity of one or more nucleic acid sequences selected from the group consisting of OB:3.

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23. The method of claim <sup>21</sup>20, wherein the agent is an antibody to a polypeptide encoded by the OB nucleic acid sequence, a peptide, peptidomimetic, small molecule, or other drug.

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24. A kit comprising one or more reagents for detecting two or more nucleic acid sequences selected from the group consisting of OBs:1-6.

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25. An array of probe nucleic acids, wherein said probe nucleic acids detect two or more nucleic acid sequences selected from the group consisting of OBs:1-6.

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26. An isolated nucleic acid molecule comprising a nucleic acid sequence that is least 75% identical to SEQ ID NO:1, or the complement of the nucleic acid sequence.

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27. A nucleic acid vector comprising the nucleic acid sequence of claim <sup>27</sup>26.

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28. A host cell comprising the isolated nucleic acid molecule of claim <sup>27</sup>26.

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29. An isolated polypeptide at least 80% identical to a polypeptide selected from the group consisting of:

- a) a polypeptide comprising an amino acid sequence encoded by the nucleic acid sequence of SEQ ID NO:1;
- b) a fragment of a polypeptide comprising an amino acid sequence encoded by the nucleic acid sequence of SEQ ID NO:1, wherein the fragment comprises at least 6 contiguous amino acids;
- c) a derivative of a polypeptide comprising an amino acid sequence encoded by the nucleic acid sequence of SEQ ID NO:1;
- d) an analog of a polypeptide comprising an amino acid sequence encoded by the nucleic acid sequence of SEQ ID NO:1; and
- e) a homolog of a polypeptide comprising an amino acid sequence encoded by the nucleic acid sequence of SEQ ID NO:1.

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30. An antibody that selectively binds to the polypeptide of claim <sup>30</sup>29, and fragments, homologs, analogs and derivatives of the antibody.

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31. A pharmaceutical composition comprising the nucleic acid of claim <sup>27</sup>26.

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A pharmaceutical composition comprising the polypeptide of claim <sup>30</sup>29.

A method of detecting the presence of the nucleic acid of claim <sup>27</sup>26 in a sample, comprising contacting the sample with a compound that selectively binds to the nucleic acid of claim <sup>27</sup>26 and determining whether the compound bound to the nucleic acid of claim <sup>27</sup>26 is present in the sample.

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A method for modulating the activity of the nucleic acid of claim <sup>27</sup>26, the method comprising contacting a cell sample comprising the nucleic acid of claim <sup>27</sup>26 with a compound that binds to said nucleic acid in an amount sufficient to modulate the activity of the polypeptide.

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An isolated polypeptide used to treat obesity in a subject, wherein the polypeptide is at least 80% identical to a polypeptide selected from the group consisting of:

- a) a polypeptide comprising an amino acid sequence of OBs:1-6;
- b) a fragment of a polypeptide comprising an amino acid sequence of OBs:1-6, wherein the fragment comprises at least 6 contiguous amino acids of OBs:1-6;
- c) a derivative of a polypeptide comprising an amino acid sequence of OBs:1-6;
- d) an analog of a polypeptide comprising an amino acid sequence of OBs:1-6; and
- e) a homolog of a polypeptide comprising an amino acid sequence of OBs:1-6.

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The polypeptide of claim <sup>36</sup>35, wherein the expression status of the polypeptide is regulated by leptin.

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The polypeptide of claim <sup>37</sup>36, wherein the expression of the polypeptide is down-regulated by leptin and the polypeptide is selected from the group consisting of OBs:1, 2, and 4-6.

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The polypeptide of claim <sup>37</sup>36, wherein the expression of the polypeptide is up-regulated by leptin and the polypeptide is selected from the groups consisting of OBs:3.

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The polypeptide of claim <sup>36</sup>35, wherein the subject is a mammal.

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The polypeptide of claim <sup>40</sup>39, wherein the subject is human.

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The polypeptide claim <sup>36</sup>35, wherein the polypeptide is secreted from the pituitary gland.

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An isolated nucleic acid molecule used to treat obesity in a subject, wherein the nucleic acid is least 75% identical to the nucleic acid sequence any one of OBs:1-6 or the complement of the nucleic acid sequence.

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43. The nucleic acid molecule of claim 43, wherein the expression status of the nucleic acid sequence is regulated by leptin.

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44. The nucleic acid molecule of claim 43, wherein the expression status of the nucleic acid sequence is down-regulated by leptin and the nucleic acid is selected from the group

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45. consisting of OBs:1,2, and 4-6.

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45. The nucleic acid molecule of claim 45, wherein the expression status of the nucleic acid sequence is up-regulated by leptin and the nucleic acid is selected from the group consisting of OBs:3.

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46. The nucleic acid molecule of claim 46 wherein the subject is a mammal.

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47. The nucleic acid molecule of claim 46 wherein the subject is human.

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48. The nucleic acid sequence of claim 47, wherein the nucleic acid sequence is expressed in the pituitary gland.

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49. A composition which is secreted by the pituitary gland, is associated with obesity, and whose expression status is modulated by leptin.

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50. The composition of claim 49, wherein the composition is selected from the group consisting of OBs:1-6.